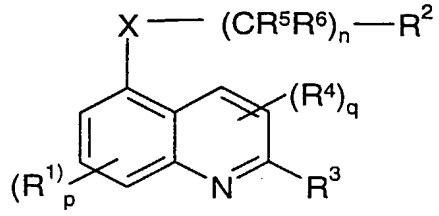
CLAIMS

1. A compound of formula



(I)

or a pharmaceutically acceptable salt or solvate thereof, wherein

p is 0, 1 or 2;

each R^1 independently represents halogen or C_1-C_6 alkyl optionally substituted by at least one substituent selected from hydroxyl, halogen and C_1-C_6 alkoxy;

X is C(O)NH or NHC(O);

n is 1, 2, 3, 4 or 5;

within each grouping, CR^5R^6, R^5 and R^6 each independently represent hydrogen, halogen, phenyl or C_1-C_6 alkyl, or R^5 and R^6 together with the carbon atom to which they are both attached form a C_3-C_8 cycloalkyl ring;

R^2 represents an unsaturated 4- to 10-membered ring system which may comprise at least one ring heteroatom selected from nitrogen, oxygen and sulphur, the ring system being optionally substituted with at least one substituent selected from halogen, $-COOR^{13}$, hydroxyl, $-NR^{14}R^{15}$, $-CONR^{16}R^{17}$, $-SO_2NR^{18}R^{19}$, $-NR^{20}SO_2R^{21}$, C_1-C_6 alkyl, C_1-C_6 alkylcarbonyl, C_1-C_6 alkoxy, C_1-C_6 alkylcarbonyloxy, C_1-C_6 alkoxycarbonyl, C_1-C_6 hydroxyalkyl and $-S(O)_mC_1$-C_6 alkyl where m is 0, 1 or 2;

R^3 represents hydrogen or a group $-R^7$, $-OR^7$, $-SR^7$ or $-NR^7R^8$;

q is 0, 1 or 2;

each R^4 independently represents halogen or C_1-C_6 alkyl optionally substituted by at least one substituent selected from hydroxyl, halogen and C_1-C_6 alkoxy;

R^7 and R^8 each independently represent hydrogen, C_1-C_{10} alkyl, C_3-C_8 cycloalkyl or a saturated or unsaturated 3- to 10-membered heterocyclic ring system comprising at least one ring heteroatom selected from nitrogen, oxygen and sulphur, the alkyl, cycloalkyl and heterocyclic ring system each being optionally substituted with at least one substituent

selected from halogen, hydroxyl, C_1-C_6 alkoxy, C_1-C_6 alkylthio, C_1-C_6 hydroxyalkyl, C_1-C_6 hydroxyalkoxy, C_1-C_6 alkoxycarbonyl, C_3-C_8 cycloalkyl, $-NR^9R^{10}$, $-COOR^{22}$, $-CONR^{23}R^{24}$, $-SO_2NR^{25}R^{26}$, $-NR^{27}SO_2R^{28}$ and ZR^{68} or

alternatively, R^7 and R^8 may together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring that optionally further comprises one or two ring heteroatoms independently selected from nitrogen, oxygen and sulphur and that optionally further comprises a bridging group, the heterocyclic ring being optionally substituted with at least one substituent selected from halogen, hydroxyl, cyano, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 alkylthio, C_1-C_6 hydroxyalkyl, C_1-C_6 hydroxyalkoxy, C_1-C_6 alkoxycarbonyl, C_3-C_8 cycloalkyl, $-NR^{11}R^{12}$, $-COOR^{29}$, $-CONR^{30}R^{31}$, $-SO_2NR^{32}R^{33}$, $-NR^{34}SO_2R^{35}$, $Z'R^{69}$, $(CH_2)_{1-6}NR^{70}R^{71}$, SO_2R^{72}, $NR^{73}CONR^{74}SO_2R^{75}$ or $M(CH_2)_{1-6}COOR^{76}$ wherein M represents a bond, O, S, SO, SO_2, and a group $>NR^{77}$;

R^9 and R^{10} each independently represent hydrogen or a C_1-C_6 alkylcarbonyl, C_2-C_7 alkenyl or C_1-C_7 alkyl group, each group being optionally substituted with at least one substituent selected from hydroxyl, $-NR^{36}R^{37}$, $-COOR^{38}$, $-CONR^{39}R^{40}$, $-SO_2NR^{41}R^{42}$, $-NR^{43}SO_2R^{44}$, C_1-C_6 alkoxy, C_1-C_6 alkylthio, C_1-C_6 alkoxycarbonyl and a saturated or unsaturated 3- to 10-membered ring system which may comprise at least one ring heteroatom selected from nitrogen, oxygen and sulphur, the ring system in turn being optionally substituted with at least one substituent selected from halogen, hydroxyl, oxo, carboxyl, cyano, C_1-C_6 alkyl and C_1-C_6 hydroxyalkyl, or

alternatively, R^9 and R^{10} may together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring that optionally further comprises one or two ring heteroatoms independently selected from nitrogen, oxygen and sulphur, the heterocyclic ring being optionally substituted with at least one substituent selected from $-OR^{54}$, $-NR^{55}R^{56}$, $-(CH_2)_t-NR^{57}R^{58}$ where t is 1, 2, 3, 4, 5 or 6, $-COOR^{59}$, $-CONR^{60}R^{61}$, $-SO_2NR^{62}R^{63}$, $-NR^{64}SO_2R^{65}$, C_1-C_6 hydroxyalkyl, C_1-C_6 alkoxy, C_1-C_6 alkylthio, C_1-C_6 alkoxycarbonyl and $Z''R^{80}$;

R^{11} and R^{12} each independently represent hydrogen or a C_1-C_6 alkylcarbonyl, C_1-C_6 alkoxycarbonyl, C_2-C_7 alkenyl or C_1-C_7 alkyl group, each group being optionally

substituted with at least one substituent selected from hydroxyl, $-NR^{45}R^{46}$, $-COOR^{47}$, $-CONR^{48}R^{49}$, $-SO_2NR^{50}R^{51}$, $-NR^{52}SO_2R^{53}$, $-NR^{66}C(O)R^{67}$, C_1-C_6 alkoxy, C_1-C_6 alkylthio and C_1-C_6 alkoxycarbonyl;

Z, Z' and Z'' independently represent a bond, O, S, SO, SO_2, $>NR^{78}$, C_{1-6} alkylene, or a group $-O(CH_2)_{1-6}-$, $-NR^{79}(CH_2)_{1-6}-$ or $-S(O)_p(CH_2)_{1-6}-$ wherein p is 0, 1 or 2;

R^{68}, R^{69} and R^{80} independently represent tetrazolyl or a 5- to 6- membered heterocyclic ring comprising from 1 to 4 heteroatoms selected from nitrogen, oxygen and sulphur, which heterocyclic ring is substituted by at least one substituent selected from hydroxyl, =O, and =S, and which heterocyclic ring may further be optionally substituted by at least one substituent selected from halogen , nitro, cyano, $-SO_2C_{1-6}$ alkyl, C_{1-6} alkoxycarbonyl, and a C_{1-6} alkyl group which C_{1-6} alkyl group can be optionally substituted by at least one substituent selected from halogen and hydroxyl;

R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18}, R^{19}, R^{20} and R^{21} each independently represent hydrogen or C_1-C_6 alkyl optionally substituted by at least one substituent selected from hydroxyl, halogen and C_1-C_6 alkoxy;

R^{22}, R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, R^{28}, R^{29}, R^{30}, R^{31}, R^{32}, R^{33}, R^{34} and R^{35} each independently represent hydrogen or C_1-C_6 alkyl optionally substituted by at least one substituent selected from hydroxyl, halogen and C_1-C_6 alkoxy;

R^{36}, R^{37}, R^{38}, R^{39}, R^{40}, R^{41}, R^{42}, R^{43}, R^{44}, R^{45}, R^{46}, R^{47}, R^{48}, R^{49}, R^{50}, R^{51}, R^{52} and R^{53} each independently represent hydrogen or C_1-C_6 alkyl optionally substituted by at least one substituent selected from hydroxyl, halogen and C_1-C_6 alkoxy;

R^{54}, R^{55}, R^{56}, R^{57}, R^{58}, R^{59}, R^{60}, R^{61}, R^{62}, R^{63}, R^{64}, R^{65}, R^{66} and R^{67} each independently represent hydrogen or C_1-C_6 alkyl optionally substituted by at least one substituent selected from hydroxyl, halogen and C_1-C_6 alkoxy; and

R^{70}, R^{71}, R^{72}, R^{73}, R^{74}, R^{75}, R^{76}, R^{77}, R^{78} and R^{79} each independently represent hydrogen or C_1-C_6 alkyl optionally substituted by at least one substituent selected from hydroxyl, halogen and C_1-C_6 alkoxy;

with the provisos that:

(a) when X represents NHC(O), p is 0, q is 0, n is 1 and R^3, R^5 and R^6 each independently represent hydrogen, then R^2 is other than a 2-carboxy-phenyl group; and

(b) when X represents NHC(O), p is 0, q is 0, n is 2, R^3 represents hydrogen and each R^5 and R^6 independently represents hydrogen, then R^2 is other than a 3,4-diamino-phenyl group or a 5-methyl-2-furanyl group; and

(c) when X represents C(O)NH, p is 0, q is 0, n is 2, R^3 represents hydrogen and each R^5 and R^6 independently represents hydrogen, then R^2 is other than an unsubstituted phenyl group, an unsubstituted 1H-indol-3-yl group, or a 2-methyl-1H-indol-3-yl group.

2. A compound according to claim 1, wherein X is NHC(O).

3. A compound according to claim 1 or claim 2, wherein R^2 represents an unsaturated 4-, 5- or 6-membered ring optionally comprising one ring heteroatom selected from nitrogen, oxygen and sulphur, the ring being optionally substituted with one, two, three or four substituents independently selected from halogen, $-COOR^{13}$, hydroxyl, $-NR^{14}R^{15}$, $-CONR^{16}R^{17}$, $-SO_2NR^{18}R^{19}$, $-NR^{20}SO_2R^{21}$, C_1-C_4 alkyl, C_1-C_4 alkylcarbonyl, C_1-C_4 alkoxy, C_1-C_4 alkylcarbonyloxy, C_1-C_4 alkoxycarbonyl, C_1-C_4 hydroxyalkyl and $-S(O)_mC_1$-C_4 alkyl where m is 0, 1 or 2.

4. A compound according to any one of the preceding claims, wherein R^3 represents hydrogen or a group $-R^7$ or $-NR^7R^8$.

5. A compound according to any one of the preceding claims wherein R^7 and R^8 each independently represent hydrogen or C_1-C_{10} alkyl optionally substituted with one or two substituents independently selected from halogen, hydroxyl, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 hydroxyalkyl, C_1-C_4 hydroxyalkoxy, C_1-C_4 alkoxycarbonyl, C_5-C_6 cycloalkyl, $-NR^9R^{10}$, $-COOR^{22}$, $-CONR^{23}R^{24}$, $-SO_2NR^{25}R^{26}$ and $-NR^{27}SO_2R^{28}$.

6. A compound according to any one of claims 1 to 4, wherein R^7 and R^8 together with the nitrogen atom to which they are attached form a 5- to 6-membered saturated heterocyclic ring that optionally further comprises a ring nitrogen atom, the heterocyclic ring being optionally substituted with one or two substituents independently selected from halogen, hydroxyl, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 hydroxyalkyl, C_1-C_4 hydroxyalkoxy, C_1-C_4 alkoxycarbonyl, C_5-C_6 cycloalkyl, $-NR^{11}R^{12}$, $-COOR^{29}$, $-CONR^{30}R^{31}$, $-SO_2NR^{32}R^{33}$ and $-NR^{34}SO_2R^{35}$.

7. A compound according to any one of the preceding claims, wherein within each grouping CR^5R^6, R^5 and R^6 each independently represent hydrogen or C_1-C_4 alkyl.

8. A compound according to claim 1 selected from:

6-Chloro-2-methyl-*N*-[(2*R*)-2-phenylpropyl]-5-quinolinecarboxamide,

6-Chloro-2-methyl-*N*-[(2*S*)-2-phenylpropyl]-5-quinolinecarboxamide,

(β*R*)-*N*-[6-Chloro-2-[methyl[3-(methylamino)propyl]amino]-5-quinolinyl]-β-methyl-benzenepropanamide,

(β*R*)-*N*-[6-Chloro-2-(1-piperazinyl)-5-quinolinyl]-β-methyl-benzenepropanamide,

6-Chloro-2-methyl-*N*-(2-phenylethyl)-5-quinolinecarboxamide,

(β*R*)-*N*-[6-Chloro-2-[3-(ethylamino)propyl]-5-quinolinyl]-β-methyl-benzenepropanamide,

(β*R*)-*N*-[6-Chloro-2-[3-[(3-hydroxypropyl)amino]propyl]-5-quinolinyl]-β-methyl-benzenepropanamide,

3,4-Dichloro-α-methyl-*N*-5-quinolinyl-benzenepropanamide,

(β*R*)-*N*-[6-Chloro-2-[[2-[(2-hydroxyethyl)amino]ethyl]amino]-5-quinolinyl]-β-methyl-benzenepropanamide,

2-Chloro-*N*-[6-chloro-2-(1-piperazinyl)-5-quinolinyl]-benzenepropanamide,

2,4-Dichloro-*N*-[6-chloro-2-(1-piperazinyl)-5-quinolinyl]-benzenepropanamide,

4-Chloro-*N*-[6-chloro-2-(1-piperazinyl)-5-quinolinyl]-benzenepropanamide,

(β*R*)-*N*-[2-[(3*S*)-3-Amino-1-pyrrolidinyl]-6-chloro-5-quinolinyl]-β-methyl-benzenepropanamide,

N-[6-Chloro-2-(1-piperazinyl)-5-quinolinyl]-2-methoxy-benzenepropanamide,

(β*R*)-*N*-[6-Chloro-2-[(3*S*)-3-[(3-hydroxypropyl)amino]-1-pyrrolidinyl]-5-quinolinyl]-β-methyl-benzenepropanamide,

(β*R*)-*N*-[6-Chloro-2-[(3S)-3-[(2-hydroxyethyl)amino]-1-pyrrolidinyl]-5-quinolinyl]-β-methyl-benzenepropanamide,

N-[6-Chloro-2-(1-piperazinyl)-5-quinolinyl]-benzenepropanamide,

N-[2-[(3*S*)-3-Amino-1-pyrrolidinyl]-6-chloro-5-quinolinyl]-2-chloro-benzenepropanamide,

2-Chloro-*N*-[6-chloro-2-[(3*S*)-3-[(2-hydroxyethyl)amino]-1-pyrrolidinyl]-5-quinolinyl]-benzenepropanamide,

1-[6-Chloro-5-[[3-(2-chlorophenyl)-1-oxopropyl]amino]-2-quinolinyl]-4-piperidinecarboxylic acid,

2-[(3*S*)-3-Amino-1-pyrrolidinyl]-6-chloro-*N*-[2-(2-chlorophenyl)ethyl]-5-quinolinecarboxamide,

6-Chloro-*N*-[2-(2-chlorophenyl)ethyl]-2-[(3*S*)-3-[(2-hydroxyethyl)amino]-1-pyrrolidinyl]-5-quinolinecarboxamide,

1-[6-Chloro-5-[[[2-(2,6-dichlorophenyl)ethyl]amino]carbonyl]-2-quinolinyl]-4-piperidinecarboxylic acid,

1-[6-Chloro-5-[[[2-(2-chlorophenyl)ethyl]amino]carbonyl]-2-quinolinyl]-4-piperidinecarboxylic acid,

1-[6-Chloro-5-[[(2,2-diphenylethyl)amino]carbonyl]-2-quinolinyl]-4-piperidinecarboxylic acid,

1-[6-Chloro-5-[[(2-phenylethyl)amino]carbonyl]-2-quinolinyl]-4-piperidinecarboxylic acid,

1-[6-Chloro-5-[[[2-(2-fluorophenyl)ethyl]amino]carbonyl]-2-quinolinyl]-4-piperidinecarboxylic acid,

1-[6-Chloro-5-[[[2-(2-methylphenyl)ethyl]amino]carbonyl]-2-quinolinyl]-4-piperidinecarboxylic acid,

1-[6-Chloro-5-[[[(2*S*)-2-phenylpropyl]amino]carbonyl]-2-quinolinyl]-4-piperidinecarboxylic acid,

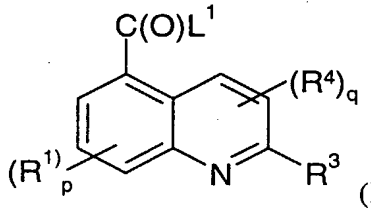
6-Chloro-*N*-[2-(2-chlorophenyl)ethyl]-2-[4-(1,5-dihydro-5-oxo-4*H*-1,2,4-triazol-4-yl)-1-piperidinyl]-5-quinolinecarboxamide, and

1-[6-Chloro-5-[[[2-(4-chlorophenyl)ethyl]amino]carbonyl]-2-quinolinyl]-4-piperidinecarboxylic acid,

and all their pharmaceutically acceptable salts and solvates.

9. A process for the preparation of a compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt or solvate thereof, which comprises

(a) reacting a compound of formula



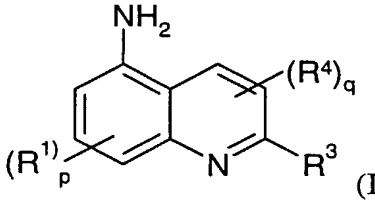
(II)

wherein L^1 represents a leaving group (e.g. hydroxyl or halogen) and p, q, R^1, R^3 and R^4 are as defined in formula (I), with a compound of formula

(III)

wherein n, R^2, R^5 and R^6 are as defined in formula (I); or

(b) reacting a compound of formula



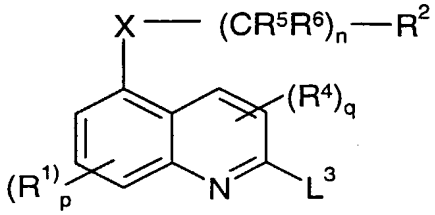
(IV)

wherein p, q, R^1, R^3 and R^4 are as defined in formula (I), with a compound of formula

(V)

wherein L^2 represents a leaving group (e.g. hydroxyl or halogen) and n, R^2, R^5 and R^6 are as defined in formula (I); or

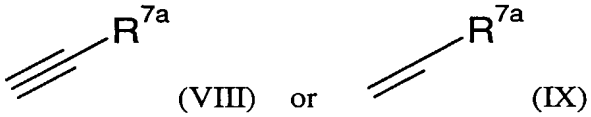
(c) when R^3 represents a group $-NR^7R^8$, reacting a compound of formula



(VI)

wherein L^3 is a leaving group (e.g. chloride, bromide, fluoride, iodide, paratoluenesulphonate or methanesulphonate) and n, p, q, X, R^1, R^2, R^4, R^5 and R^6 are as defined in formula (I), with a compound of formula (VII), $H\text{-}NR^7R^8$, wherein R^7 and R^8 are as defined in formula (I); or

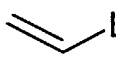
(d) when R^3 represents a group R^7 where R^7 is an optionally substituted C_3-C_{10} alkyl group, reacting a compound of formula (VI) as defined in (c) above with a compound of formula



(VIII) or (IX)

wherein R^{7a} represents a C_1-C_8 alkyl group optionally substituted as defined for R^7 in formula (I), optionally followed by a hydrogenation reaction; or

(e) when R^3 represents a group R^7 where R^7 is $-(CH_2)_2NR^9R^{10}$, reacting a compound of formula (VI) as defined in (c) above with a compound of formula



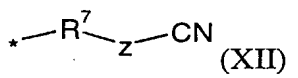
(X)

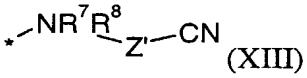
wherein L^4 is a leaving group (eg. trialkyltin, dialkylboron or zinc), followed by reaction with a compound of formula (XI), HNR^9R^{10}, wherein R^9 and R^{10} are as defined in formula (I); or

(f) when R^3 represents a group R^7 where R^7 is $-CH_2NR^9R^{10}$, reacting a compound of formula (VI) as defined in (c) above with a compound of formula (X) as defined in (e)

above, followed by an oxidation reaction and then by reaction with a compound of formula (XI) as defined in (e) above under reductive amination conditions; or

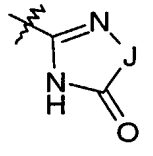
(g) when R^3 represents a group R^7ZR^{68} or NR^7R^8 wherein R^7 and/or R^8 are substituted by a group $Z'R^{69}$ or R^7 and R^8 together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclic ring substituted by a group $Z'R^{69}$, and R^{68} or R^{69} is tetrazolyl, reacting a group of formula (XII) or (XIII)


(XII)


(XIII)

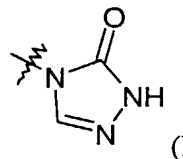
with a compound of formula GN_3, wherein G is sodium, a trialkylsilyl, an alkyltin or ammonium, to yield a group of formula I wherein R^7, R^8, Z, Z' are as defined in formula (I); or

(h) when R^3 represents a group R^7ZR^{68} or NR^7R^8 wherein R^7 and/or R^8 are substituted by a group $Z'R^{69}$ or R^7 and R^8 together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclic ring substituted by a group $Z'R^{69}$, and R^{68} or R^{69} is group of formula


(XIV)

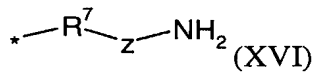
reacting a compound of formula XII or XIII wherein XII or XIII are as defined in (g) above with hydroxylamine, followed by treatment with 1,1'-thiocarbonyldiimidazole and subsequent treatment with silica gives a group of formula (XIV) wherein J is S, alternatively reacting a compound of formula XII or XIII wherein XIII or XIII are as defined in (g) above with hydroxylamine, followed by treatment with a suitable chloroformate gives a group of formula (XIV) wherein J is O; or

(i) when R^3 represents a group R^7ZR^{68} or NR^7R^8 wherein R^7 and/or R^8 are substituted by a group $Z'R^{69}$ or R^7 and R^8 together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclic ring substituted by a group $Z'R^{69}$, and R^{68} or R^{69} is

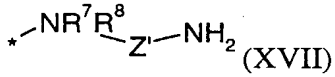


(XV)

reacting a compound of formula XVI or XVII



(XVI)



(XVII)

with a source of phosgene followed by treatment with formyl hydrazine and subsequent treatment with base;

and optionally after (a), (b), (c), (d), (e), (f), (g), (h) or (i) carrying out one or more of the following:

- converting the compound obtained to a further compound of the invention
- forming a pharmaceutically acceptable salt or solvate of the compound.

10. A compound of formula (VI) as defined in claim 9.

11. (β*R*)-*N*-(2,6-Dichloro-5-quinolinyl)-β-methyl-benzenepropanamide.

12. A pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as claimed in any one of claims 1 to 8 in association with a pharmaceutically acceptable adjuvant, diluent or carrier.

13. A process for the preparation of a pharmaceutical composition as claimed in claim 12 which comprises mixing a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as defined in any one of claims 1 to 8 with a pharmaceutically acceptable adjuvant, diluent or carrier.

14. A compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as claimed in any one of claims 1 to 8 for use in therapy.

15. Use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as claimed in any one of claims 1 to 8 in the manufacture of a medicament for use in the treatment of rheumatoid arthritis.

16. Use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as claimed in any one of claims 1 to 8 in the manufacture of a medicament for use in the treatment of an obstructive airways disease.

17. Use according to claim 16, wherein the obstructive airways disease is asthma or chronic obstructive pulmonary disease.

18. Use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as claimed in any one of claims 1 to 8 in the manufacture of a medicament for use in the treatment of osteoarthritis.

19. Use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as claimed in any one of claims 1 to 8 in the manufacture of a medicament for use in the treatment of atherosclerosis.

20. A method of treating rheumatoid arthritis or osteoarthritis which comprises administering to a patient a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as claimed in any one of claims 1 to 8.

21. A method of treating an obstructive airways disease which comprises administering to a patient a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof as claimed in any one of claims 1 to 8.